Bayer HealthCare
Consumer Care Division

January 28, 2005

Division of Dockets Management
5630 Fishers Lane Rm. 1061
Rockville, MD 20852

Re: **Docket No 1976N-0052N**
RIN 0910-AF34
Cold, Cough, Allergy, Bronchodilator, and Antiasthmatic Drug Products for Over-the-Counter Human Use; Proposed Amendment of Monograph for Over-the-Counter Nasal Decongestant Products

Bayer HealthCare LLC
Consumer Care Division
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Dear Sir or Madam:

In the November 2, 2004 Federal Register, the Food and Drug Administration (FDA) published and solicited comments on a proposed rule entitled "Cold, Cough, Allergy, Bronchodilator, and Antiasthmatic Drug Products for Over-the-Counter Human Use; Proposed Amendment of Monograph for Over-the-Counter Nasal Decongestant Products" (referred to in this document as the "Proposed Rule"). The Proposed Rule would add phenylephrine bitartrate (PEB) as a generally recognized as safe and effective (GRASE) nasal decongestant ingredient when used in an effervescent tablet as a single ingredient or in combination with aspirin and chlorpheniramine maleate.

Bayer HealthCare supports FDA's recommendation to add phenylephrine bitartrate to the monograph for over-the-counter nasal decongestants. However, we ask that the Agency consider the following two proposals and supportive information as detailed below:

1. Expand the definition of an effervescent dosage form to provide greater formulation flexibility to manufacturers
2. Permit the inclusion of phenylephrine bitartrate as an allowable oral nasal decongestant ingredient, when formulated in an effervescent tablet, in all combinations containing an oral nasal decongestant when labeled in accordance with 21 CFR 341.80 and 21 CFR 341.85.

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Proposal #1: Expand the definition of an effervescent dosage form.

On pages 63486 to 63487 of the Proposed Rule, the following definition was proposed for an effervescent tablet:

Definition as proposed by the Agency 21 CFR 341.3(l)
Effervescent tablet: A tablet intended to be dissolved in water before administration. It contains, in addition to the active ingredient(s), mixtures of acids (citric acid, tartaric acid) and sodium bicarbonate, which releases carbon dioxide when dissolved in water.

Bayer suggests the following revised definition for an effervescent tablet (changes to the proposed definition are bolded) which takes into consideration definitions from 21 CFR, United States Pharmacopeia (USP), British/European Pharmacopeia (BP/EP), as well as many pharmaceutical texts and reference books, including pharmacopeial individual monographs. The revisions suggested will avoid placing limitations on companies attempting to formulate effervescent dosage forms.

Proposed Revised Definition of an Effervescent Tablet:
Effervescent tablet: A tablet intended to be dissolved **or dispersed** in water before administration. It **generally** contains, in addition to the active ingredient(s), mixtures of acids/acid salts (citric acid, tartaric acid, **malic acid, or any other suitable acid or acid anhydride...) and carbonates or hydrogen carbonates (Sodium, potassium, or any other suitable alkali metal carbonate or hydrogen carbonate**), which release carbon dioxide when *mixed with* water. **Occasionally, the active ingredient itself could act as the acid or alkali metal compound necessary for effervescent reaction.**

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References:

1. USP 27-NF 22 S2: Effervescent Tablet, Definition

Soluble, effervescent tablets are prepared by compression and contain, in addition to active ingredients, mixtures of acids (citric acid, tartaric acid) and sodium bicarbonate, which release carbon dioxide when dissolved in water. They are intended to be dissolved or dispersed in water before administration. Effervescent tablets should be stored in tightly closed containers or moisture-proof packs and labeled to indicate that they are not to be swallowed directly.

Examples of USP Effervescent Tablet Monographs

Aspirin Effervescent Tablets for Oral Solution

Aspirin Effervescent Tablets for Oral Solution contain Aspirin and an effervescent mixture of a suitable organic acid and alkali metal bicarbonate and/or carbonate. Tablets contain not less than 90.0 percent and not more than 110.0 percent of the labeled amount of C9H8O4.

Potassium Bicarbonate Effervescent Tablets for Oral Solution

Potassium Bicarbonate Effervescent Tablets for Oral Solution contain not less than 90.0 percent and not more than 110.0 percent of the labeled amount of K.

Potassium Bicarbonate and Potassium Chloride Effervescent Tablets for Oral Solution

Potassium Bicarbonate and Potassium Chloride Effervescent Tablets for Oral Solution contain not less than 90.0 percent and not more than 110.0 percent of the labeled amounts of K and Cl.

Potassium and Sodium Bicarbonates and Citric Acid Effervescent Tablets for Oral Solution

Potassium and Sodium Bicarbonates and Citric Acid Effervescent Tablets for Oral Solution contain not less than 90.0 percent and not more than 110.0 percent of the labeled amounts of potassium bicarbonate (KHCO3), sodium bicarbonate (NaHCO3), and anhydrous citric acid (C6H8O7).

Potassium Chloride, Potassium Bicarbonate, and Potassium Citrate Effervescent Tablets for Oral Solution

Potassium Chloride, Potassium Bicarbonate, and Potassium Citrate Effervescent Tablets for Oral Solution contain not less than 90.0 percent and not more than 110.0 percent of the labeled amounts of K and Cl.

References (continued):

2. BP 2003 / EP: Effervescent Tablets, EP Definition

Effervescent tablets are uncoated tablets generally containing acid substances and carbonates or hydrogen carbonates which react rapidly in the presence of water to release carbon dioxide. They are intended to be dissolved or dispersed in water before administration.

3. Modern Pharmaceutics, Banker and Rhodes, 2nd Addition Revised and Extended

The basic ingredient of any effervescent product is an acidic material in combination with a dry carbonate salt. The acidity is derived from.... (citric, tartaric acid, malic acid), acid anhydrides (succinic anhydride), and acid salts (sodium dihydrogen phosphate, disodium dihydrogen pyrophosphate) ..... Carbonates sources include sodium or potassium bicarbonate or carbonate and more recently, sodium glycine carbonate.

4. The Theory and Practice of Industrial Pharmacy, Lachman, Lieberman, Kanig

Effervescent Tablets... the use of chemical reaction to produce carbon dioxide...The combination of alkali metal carbonates and bicarbonate with tartaric or citric acid produces this reaction in water.

5. Handbook of Pharmaceutical Excipients, 2003

Components used in Effervescent Tablet: Citric acid anhydrous, citric acid monohydrate, tartaric acid, dextrates, fumaric acid, sodium citrate dihydrate, sodium bicarbonate, potassium bicarbonate.

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Proposal #2: Permit the inclusion of phenylephrine bitartrate as an allowable oral nasal decongestant, when formulated in an effervescent tablet, in all combinations containing an oral nasal decongestant when labeled in accordance with 21 CFR 341.80 and 21 CFR 341.85.

On page 63488 of the Proposed Rule, FDA proposed the following:

341.40(cc): phenylephrine bitartrate identified in 341.20(a)(4) may be combined with chlorpheniramine maleate identified in 341.12(c) and aspirin provided the product is available only in an effervescent tablet and provided that the product is labeled according to 341.85.

No other cold-cough combinations containing phenylephrine bitartrate in an effervescent tablet were recognized in the Proposed Rule.

Bayer asks that the Agency include phenylephrine bitartrate as a GRASE nasal decongestant in all permissible combinations containing an oral nasal decongestant when formulated in an effervescent tablet. Our proposal is based on the following:

- Another phenylephrine salt, phenylephrine hydrochloride (PEH), is included as a GRASE oral nasal decongestant ingredient in the Cold, Cough, Allergy, Bronchodilator, and Antiasthmatic Drug Products for Over-the-Counter Human Use OTC monograph. It is included in 17 permitted combinations {see 21 CFR 341.40 (b)(c)(e)(g)(l)(j)(m)(n)(p)(q)(r)(s)(t)(x)(y)(aa) and (bb)}.

- It was concluded by the Agency in the Proposed Rule that "both phenylephrine salts have the same pharmacologic activity and similar side effects", and "the two phenylephrine salts (bitartrate and hydrochloride) appear to have comparable bioavailability" when presented in an effervescent tablet.

- FDA acknowledged in the Proposed Rule that "the two salts of phenylephrine could be used in the effervescent tablets interchangeably without any clinically significant impact on the performance of the formulations studied."

- According to the CDER's Guidance for Industry – Bioavailability and Bioequivalence Studies for Orally Administered Products General Considerations (March 2003); "in vivo BA and/or BE studies for oral solutions, elixirs, syrups, tinctures, or other solubilized forms, can be waived (21 CFR 320.22(b)(3)(i)). Generally, in vivo BE studies are waived for solutions on the assumption that release of the drug substance from the drug product is self-evident and that the solutions do not contain any excipient that significantly affects drug absorption (21 CFR 320.22(b)(3)(iii))".

- Provided in this submission are *in vitro* data intended to demonstrate that once dissolved, the phenylephrine base in solution is virtually indistinguishable regardless of the salt form. The presence or absence of other common cough/cold active ingredients in the solution, such as aspirin (ASA), acetaminophen (APAP), chlorpheniramine, etc., appear to have no significant effect on the pH of the solution or the solubility of the individual ingredients.

Design of the *in-vitro* experiment:

Five (5) of Bayer's currently marketed effervescent Cough-Cold formulations that contain an acetaminophen/phenylephrine hydrochloride base were compared to five (5) proposed combinations containing an aspirin/phenylephrine bitartrate base and five (5) proposed combinations containing an acetaminophen/phenylephrine bitartrate base.

The *in vitro* experiment was designed to compare the impact of other cough-cold ingredients on the pH of the resulting solution and solubility of the two phenylephrine salts. Tests included pH measurement in a buffered solution and as well as a buffered solution plus 100 mL of 0.1 N hydrochloric acid solution.

Results:

The mean results of pH determinations are presented in Table 1 (APAP / PEH based formulations, currently being marketed), Table 2 (proposed ASA / PEB based formulations) and Table 3 (proposed APAP / PEB based formulations). The data in Table 1 vs. Tables 2 and 3 indicate similar pH values suggesting that the quantity of phenylephrine base in solution will be virtually the same regardless of the salt form. In addition, the data within each Table (Tables 1, 2 or 3) suggest that pH is not significantly influenced by addition or deletion of other GRASE cough – cold drug substances.

The average solubility data is shown in Tables 4 – 9. The recovery of Phenylephrine (hydrochloride or bitartrate), Analgesic (Acetaminophen or Aspirin), and the GRASE cough/cold active ingredients (chlorpheniramine maleate, doxylamine succinate and dextromethorphan) in all samples were comparable.

CONCLUSION

Bayer is asking the Agency to:

1) Broaden its proposed definition of an effervescent dosage form in order to provide more formulation flexibility with respect to inactive ingredients.

2) Include phenylephrine bitartrate in the Monograph for Over-the-Counter Nasal Decongestant Products for use in all combination products containing an oral nasal decongestant when formulated as an effervescent product based on:

- The FDA's acknowledgment that both phenylephrine salts have similar safety and efficacy profiles, and could be used in effervescent tablets interchangeably without any clinically significant impact on the performance of the formulations studied
- *In-vitro* data demonstrating that both salts are virtually indistinguishable when dissolved in a buffered solution, regardless of the presence or absence of other common cough/cold active ingredients.

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We at Bayer HealthCare appreciate the opportunity to submit comments in response to this Proposed Rule and hope that the Agency finds these comments useful as it works toward its finalization. If you have any questions regarding the content of this submission, please contact the undersigned at 973-408-8181, or in my absence, Bill Walsh at 973-408-8046.

Sincerely,

Linda Bowen

Linda F. Bowen
Associate Director, Regulatory Affairs
Bayer HealthCare LLC, Consumer Care Division

Table 1: Solution pH of Acetaminophen/PEH Formulations- Currently marketed Alka-Seltzer Plus formulations

INGREDIENTS	***Dose Weight (mg)***	**pH of Buffered Solution**	
			With 100 mL of 0.1N HCl
Sodium Bicarbonate (88%) Citric Acid Acetaminophen (APAP)	3800.0 2000.0 500.0	6.7	6.1
Sodium Bicarbonate (88%) Citric Acid Acetaminophen (APAP) PEH	3800.0 2000.0 500.0 10.0	6.7	6.0
Sodium Bicarbonate (88%) Citric Acid Acetaminophen (APAP) PEH CPM	3800.0 2000.0 500.0 10.0 4.00	6.7	6.0
Sodium Bicarbonate (88%) Citric Acid Acetaminophen (APAP) PEH CPM DEX	3800.0 2000.0 500.0 10.0 4.00 20.0	7.0	6.1
Sodium Bicarbonate (88%) Citric Acid Acetaminophen (APAP) PEH DEX	3800.0 2000.0 500.0 10.0 20.0	6.9	6.1
Sodium Bicarbonate (88%) Citric Acid Acetaminophen (APAP) PEH DOX DEX	3800.0 2000.0 500.0 10.0 12.5 20.0	6.7	6.1

Abbreviations:

CPM: chlorpheniramine maleate
DEX: dextromethorphan
DOX: doxylamine succinate
PEB: phenylephrine bitartrate
PEH: phenylephrine hydrochloride

Table 2: Solution pH of Aspirin/PEB Formulations

INGREDIENTS	***Dose Weight (mg)***	**pH of Buffered Solution**	
			With 100 mL of 0.1N HCl
Sodium Bicarbonate (88%) Citric Acid Aspirin (ASA)	3800.0 2000.0 650.0	6.8	6.0
Sodium Bicarbonate (88%) Citric Acid Aspirin (ASA) PEB	3800.0 2000.0 650.0 15.6	6.8	6.1
Sodium Bicarbonate (88%) Citric Acid Aspirin (ASA) PEB CPM	3800.0 2000.0 650.0 15.6 4.00	6.8	6.0
Sodium Bicarbonate (88%) Citric Acid Aspirin (ASA) PEB CPM DEX	3800.0 2000.0 650.0 15.6 4.00 20.0	6.8	6.0
Sodium Bicarbonate (88%) Citric Acid Aspirin (ASA) PEB DEX	3800.0 2000.0 650.0 15.6 20.0	6.9	6.0
Sodium Bicarbonate (88%) Citric Acid Aspirin (ASA) PEB DOX DEX	3800.0 2000.0 650.0 15.6 12.5 20.0	6.8	6.0

Abbreviations:

CPM: chlorpheniramine maleate
DEX: dextromethorphan
DOX: doxylamine succinate
PEB: phenylephrine bitartrate
PEH: phenylephrine hydrochloride

Table 3: Solution pH of Acetaminophen/PEB Formulations

INGREDIENTS	***Dose Weight (mg)***	**pH of Buffered Solution**	
			With 100 mL of 0.1N HCl
Sodium Bicarbonate (88%) Citric Acid Acetaminophen (APAP)	3800.0 2000.0 650.0	7.1	6.2
Sodium Bicarbonate (88%) Citric Acid Acetaminophen (APAP) PEB	3800.0 2000.0 650.0 15.6	7.0	6.2
Sodium Bicarbonate (88%) Citric Acid Acetaminophen (APAP) PEB CPM	3800.0 2000.0 650.0 15.6 4.00	7.0	6.2
Sodium Bicarbonate (88%) Citric Acid Acetaminophen (APAP) PEB CPM DEX	3800.0 2000.0 650.0 15.6 4.00 20.0	7.1	6.3
Sodium Bicarbonate (88%) Citric Acid Acetaminophen (APAP) PEB DEX	3800.0 2000.0 650.0 15.6 20.0	7.0	6.2
Sodium Bicarbonate (88%) Citric Acid Acetaminophen (APAP) PEB DOX DEX	3800.0 2000.0 650.0 15.6 12.5 20.0	7.1	6.2

Abbreviations:

CPM: chlorpheniramine maleate
DEX: dextromethorphan
DOX: doxylamine succinate
PEB: phenylephrine bitartrate
PEH: phenylephrine hydrochloride

Table 4: % Recovery of Active Ingredients in Acetaminophen/PEH Formulations – Buffer Solution (Currently Marketed Alka-Seltzer Plus Formulations)

INGREDIENTS	*Dose Weight (mg)*	% RECOVERED in Buffered Solution				
		APAP	PEH	*CPM*	*DEX*	*DOX*
Sodium Bicarbonate (88%) Citric Acid Acetaminophen (APAP)	3800.0 2000.0 500.0	98.1				
Sodium Bicarbonate (88%) Citric Acid Acetaminophen (APAP) PEH	3800.0 2000.0 500.0 10.0	98.5	100.1			
Sodium Bicarbonate (88%) Citric Acid Acetaminophen (APAP) PEH CPM	3800.0 2000.0 500.0 10.0 4.00	97.6	99.7	99.0		
Sodium Bicarbonate (88%) Citric Acid Acetaminophen (APAP) PEH CPM DEX	3800.0 2000.0 500.0 10.0 4.00 20.0	98.6	100.1	100.2	99.6	
Sodium Bicarbonate (88%) Citric Acid Acetaminophen (APAP) PEH DEX	3800.0 2000.0 500.0 10.0 20.0	99.1	99.8		99.7	
Sodium Bicarbonate (88%) Citric Acid Acetaminophen (APAP) PEH DOX DEX	3800.0 2000.0 500.0 10.0 12.5 20.0	99.4	99.9		96.2	99.3

Abbreviations:

CPM: chlorpheniramine maleate
DEX: dextromethorphan
DOX: doxylamine succinate
PEB. phenylephrine bitartrate
PEH: phenylephrine hydrochloride

Table 5: % Recovery of Active Ingredients in Acetaminophen/PEH Formulations – Acidified Buffer Solution (Currently Marketed Alka-Seltzer Plus Formulations)

INGREDIENTS	*Dose Weight (mg)*	% RECOVERED in Buffered Solution with 100mL 0.1N HCl				
		APAP	PEH	*CPM*	*DEX*	*DOX*
Sodium Bicarbonate (88%) Citric Acid Acetaminophen (APAP)	3800.0 2000.0 500.0	98.8				
Sodium Bicarbonate (88%) Citric Acid Acetaminophen (APAP) PEH	3800.0 2000.0 500.0 10.0	99.2	100.7			
Sodium Bicarbonate (88%) Citric Acid Acetaminophen (APAP) PEH CPM	3800.0 2000.0 500.0 10.0 4.00	98.4	99.8	100.4		
Sodium Bicarbonate (88%) Citric Acid Acetaminophen (APAP) PEH CPM DEX	3800.0 2000.0 500.0 10.0 4.00 20.0	97.8	99.8	99.3	96.6	
Sodium Bicarbonate (88%) Citric Acid Acetaminophen (APAP) PEH DEX	3800.0 2000.0 500.0 10.0 20.0	97.6	99.7		96.4	
Sodium Bicarbonate (88%) Citric Acid Acetaminophen (APAP) PEH DOX DEX	3800.0 2000.0 500.0 10.0 12.5 20.0	97.8	99.9		96.2	97.7

Table 6-: % Recovery of Active Ingredients in Aspirin/PEB Formulations –Buffer Solution

INGREDIENTS	*Dose Weight (mg)*	% RECOVERED in Buffered Solution				
		ASA	PEB	CPM	DEX	DOX
Sodium Bicarbonate (88%) Citric Acid Aspirin (ASA)	3800.0 2000.0 650.0	100.6				
Sodium Bicarbonate (88%) Citric Acid Aspirin (ASA) PEB	3800.0 2000.0 650.0 15.6	99.6	100.9			
Sodium Bicarbonate (88%) Citric Acid Aspirin (ASA) PEB CPM	3800.0 2000.0 650.0 15.6 4.00	98.5	101.0	100.3		
Sodium Bicarbonate (88%) Citric Acid Aspirin (ASA) PEB CPM DEX	3800.0 2000.0 650.0 15.6 4.00 20.0	100.1	100.5	100.0	100.0	
Sodium Bicarbonate (88%) Citric Acid Aspirin (ASA) PEB DEX	3800.0 2000.0 650.0 15.6 20.0	100.2	100.1		99.5	
Sodium Bicarbonate (88%) Citric Acid Aspirin (ASA) PEB DOX DEX	3800.0 2000.0 650.0 15.6 12.5 20.0	99.7	100.2		99.6	100.0

Abbreviations:

CPM: chlorpheniramine maleate
DEX: dextromethorphan
DOX: doxylamine succinate
PEB: phenylephrine bitartrate
PEH: phenylephrine hydrochloride

Table 7: % Recovery of Active Ingredients in Aspirin/PEB Formulations – Acidified Buffer Solution

INGREDIENTS	*Dose Weight (mg)*	% RECOVERED in Buffered Solution with 100mL 0.1N HCl				
		ASA	**PEB**	**CPM**	**DEX**	**DOX**
Sodium Bicarbonate (88%) Citric Acid Aspirin (ASA)	3800.0 2000.0 650.0	100.1				
Sodium Bicarbonate (88%) Citric Acid Aspirin (ASA) PEB	3800.0 2000.0 650.0 15.6	102.0	100.1			
Sodium Bicarbonate (88%) Citric Acid Aspirin (ASA) PEB CPM	3800.0 2000.0 650.0 15.6 4.00	101.7	99.9	100.9		
Sodium Bicarbonate (88%) Citric Acid Aspirin (ASA) PEB CPM DEX	3800.0 2000.0 650.0 15.6 4.00 20.0	100.7	99.7	101.0	99.8	
Sodium Bicarbonate (88%) Citric Acid Aspirin (ASA) PEB DEX	3800.0 2000.0 650.0 15.6 20.0	100.9	99.2		99.3	
Sodium Bicarbonate (88%) Citric Acid Aspirin (ASA) PEB DOX DEX	3800.0 2000.0 650.0 15.6 12.5 20.0	100.3	99.6		100.0	100.3

Abbreviations:

CPM: chlorpheniramine maleate
DEX: dextromethorphan
DOX: doxylamine succinate
PEB: phenylephrine bitartrate
PEH: phenylephrine hydrochloride

Table 8: % Recovery of Active Ingredients in Acetaminophen/PEB Formulations – Buffer Solution

INGREDIENTS	***Dose Weight (mg)***	**% RECOVERED in Buffered Solution**				
		APAP	**PEB**	***CPM***	***DEX***	***DOX***
Sodium Bicarbonate (88%) Citric Acid Acetaminophen (APAP)	3800.0 2000.0 650.0	101.1				
Sodium Bicarbonate (88%) Citric Acid Acetaminophen (APAP) PEB	3800.0 2000.0 650.0 15.6	101.2	99.5			
Sodium Bicarbonate (88%) Citric Acid Acetaminophen (APAP) PEB CPM	3800.0 2000.0 650.0 15.6 4.00	101.1	100.6	99.6		
Sodium Bicarbonate (88%) Citric Acid Acetaminophen (APAP) PEB CPM DEX	3800.0 2000.0 650.0 15.6 4.00 20.0	100.6	99.9	99.7	99.5	
Sodium Bicarbonate (88%) Citric Acid Acetaminophen (APAP) PEB DEX	3800.0 2000.0 650.0 15.6 20.0	100.5	100.0		99.8	
Sodium Bicarbonate (88%) Citric Acid Acetaminophen (APAP) PEB DOX DEX	3800.0 2000.0 650.0 15.6 12.5 20.0	100.9	99.8		99.8	100.9

Abbreviations:

CPM: chlorpheniramine maleate
DEX: dextromethorphan
DOX: doxylamine succinate
PEB: phenylephrine bitartrate
PEH: phenylephrine hydrochloride

Table 9: % Recovery of Active Ingredients in Acetaminophen/PEB Formulations – Acidified Buffer Solution

INGREDIENTS	*Dose Weight (mg)*	% RECOVERED in Buffered Solution with 100mL 0.1N HCl				
		APAP	PEB	*CPM*	*DEX*	*DOX*
Sodium Bicarbonate (88%) Citric Acid Acetaminophen (APAP)	3800.0 2000.0 650.0	95.9				
Sodium Bicarbonate (88%) Citric Acid Acetaminophen (APAP) PEB	3800.0 2000.0 650.0 15.6	96.1	97.8			
Sodium Bicarbonate (88%) Citric Acid Acetaminophen (APAP) PEB CPM	3800.0 2000.0 650.0 15.6 4.00	96.2	98.8	97.6		
Sodium Bicarbonate (88%) Citric Acid Acetaminophen (APAP) PEB CPM DEX	3800.0 2000.0 650.0 15.6 4.00 20.0	95.9	97.9	97.9	97.8	
Sodium Bicarbonate (88%) Citric Acid Acetaminophen (APAP) PEB DEX	3800.0 2000.0 650.0 15.6 20.0	95.8	98.1		98.2	
Sodium Bicarbonate (88%) Citric Acid Acetaminophen (APAP) PEB DOX DEX	3800.0 2000.0 650.0 15.6 12.5 20.0	96.1	98.1		98.0	98.1

Abbreviations:

CPM: chlorpheniramine maleate
DEX: dextromethorphan
DOX: doxylamine succinate
PEB: phenylephrine bitartrate
PEH: phenylephrine hydrochloride